CHAPTER 9
Cyanosis

KEY TEACHING POINTS

- Cyanosis results from increased amounts of bluish-colored hemoglobin in the superficial vessels of the skin. The usual cause is increased deoxyhemoglobin; rare causes are increased methemoglobin or other abnormal hemoglobins.
- The blue color of cyanosis requires a minimum *absolute* amount of abnormal hemoglobin (i.e., >2.38 g/dL arterial deoxyhemoglobin). This explains why polycythemic patients develop cyanosis more easily than anemic patients.
- Cyanosis is either *central* or *peripheral*, a distinction made at the bedside. This distinction, in turn, implies specific etiologies.
- In patients with chronic liver disease, the finding of cyanosis increases the probability of hepatopulmonary syndrome.
- Pseudocyanosis, unlike cyanosis, does not blanch with pressure, a finding indicating the color is not from abnormally colored blood but instead from abnormal pigments in the skin (e.g., silver, amiodarone).

I. DEFINITIONS

Cyanosis is an abnormal bluish discoloration of the skin and mucous membranes, caused by blue-colored blood circulating in the superficial capillaries and venules. The blue color usually represents excessive amounts of deoxygenated hemoglobin, although in some patients, it results from increased amounts of methemoglobin or sulfhemoglobin. Cyanosis may be *central* or *peripheral*. In **central cyanosis**, the blood leaving the heart is colored blue; in **peripheral cyanosis**, the blood leaving the heart is red but becomes blue by the time it reaches the fingers and toes. **Pseudocyanosis**, in contrast, refers to a permanent bluish discoloration caused by deposition of blue pigments in the skin.

Cyanosis was first described in 1761 by Morgagni, who attributed it to pulmonic stenosis.[1] In 1869, Claude Bernard described the qualitative difference in blood gases between blue venous blood and red arterial blood. The first person to quantify how much deoxygenated hemoglobin was necessary to produce the blue color was Lundsgaard in 1919.[1]

II. PATHOGENESIS

A. THE BLUE COLOR

Blood becomes blue when an absolute amount of blue pigment (usually deoxyhemoglobin) accumulates, probably because only then is the blue color deep enough to be seen through the opaque epidermis.[1-4] Once this minimal amount of

deoxyhemoglobin accumulates and cyanosis appears, the amount of additional red blood (or oxyhemoglobin) matters little to the overall skin color.

The color of the skin depends on the color of blood flowing through the dermal capillaries and subpapillary venous plexus, not the arteries and veins that lie too deep to contribute to skin color.[1,5] There has been much confusion over the absolute concentration of deoxyhemoglobin required for cyanosis, primarily because some investigators have mistakenly equated arterial levels of deoxyhemoglobin, which are easy to measure, with capillary levels, which impart the blue color but must be higher than the measured arterial levels. In patients with central cyanosis, the *average* amount of *arterial* deoxyhemoglobin is 3.48 ± 0.55 g/dL (or 5.35 g/dL in the capillaries and small venules). The *minimal* amount of *arterial* deoxyhemoglobin causing cyanosis is 2.38 g/dL (or 4.25 g/dL in the capillaries and small venules).[4]*

Because cyanosis depends on the absolute quantity of deoxyhemoglobin, not the relative amount, the appearance of cyanosis also depends on the patient's total hemoglobin concentration (i.e., 5 g/dL of capillary deoxyhemoglobin represents a higher percent of oxygen desaturation for an anemic patient, who has less total hemoglobin, than it does for a polycythemic patient). Table 9.1 displays this relationship: polycythemic patients (hemoglobin = 20 g/dL) may appear cyanotic with only mild hypoxemia (i.e., oxygen saturation [SaO_2] = 88% or pO_2 = 56 mm Hg), yet anemic patients (hemoglobin = 8 g/dL) do not develop the finding until hypoxemia is severe (i.e., SaO_2 = 70% or pO_2 = 36 mm Hg).†

TABLE 9.1 Cyanosis and Hemoglobin Concentration

	CYANOSIS APPEARS AT*	
Hemoglobin Concentration (g/dL)	Oxygen Saturation (%) Below	Arterial pO_2 (mm Hg) Below
6	60	31
8	70	36
10	76	40
12	80	45
14	83	47
16	85	50
18	87	54
20	88	56

*These figures assume that central cyanosis begins to appear when 2.38 g/dL deoxygenated hemoglobin accumulates in arterial blood (see the text for calculations). The corresponding pO_2 was obtained from standard hemoglobin dissociation curves for oxygen.

*Capillary deoxyhemoglobin is 1.87 g/dL more than arterial levels, based on three assumptions: (1) the difference in oxygen content between the arteries and veins is 5 mL of oxygen/dL blood; (2) the amount of deoxyhemoglobin in the capillaries is midway between that of the arteries and vein; and (3) 1.34 mL of oxygen binds to 1 g of saturated hemoglobin. Therefore $5/(2 \times 1.34) = 1.87$.

†These figures are calculated as follows: for the polycythemic patient (hemoglobin = 20 g/dL), 2.38 g/dL of arterial deoxyhemoglobin indicates that there is 20 − 2.38, or 17.62, g/dL of arterial oxyhemoglobin. Oxygen saturation, therefore, is (17.62)/(20) = 0.88, or 88%. For the anemic patient, the calculation is (8 − 2.38)/8 = 0.7, or 70% saturation.

B. PERIPHERAL CYANOSIS

In peripheral cyanosis, blood leaving the heart is red, but because of increased extraction of oxygen by peripheral tissues, enough deoxyhemoglobin accumulates to render it blue in the subepidermal blood vessels of the feet and hands. The clinician can easily demonstrate peripheral cyanosis by wrapping a rubber band around a finger and watching the distal digit turn blue as oxygen continues to be extracted from the stagnant blood.

III. THE FINDING

Cyanosis is best appreciated in areas where the overlying epidermis is thin and subepidermal vessels are abundant, such as the lips, nose, cheeks, ears, hands, feet, and the mucous membranes of the oral cavity.[1,6] Cyanosis is detected more easily with fluorescent lighting than with incandescent lighting or daylight.[4]

A. CENTRAL CYANOSIS

Patients with central cyanosis have blue discoloration of the lips, tongue, and sublingual tissues, as well as the hands and feet. The correlation between severity of oxygen desaturation and depth of cyanotic color is best appreciated when examining the patient's lips and buccal mucosa.[7,8] Some patients with longstanding central cyanosis have associated clubbing (see Chapter 28).

When central cyanosis is suspected but administration of oxygen fails to diminish the blue color, the clinician should consider methemoglobinemia or sulfhemoglobinemia. The color of patients with methemoglobinemia often has a characteristic brownish hue (**chocolate cyanosis**).[9]

Because cyanosis depends on blue blood being present in the underlying blood vessels, maneuvers that express blood out of the vessels (e.g., pressure on the skin) make the blue color temporarily disappear.

B. PERIPHERAL CYANOSIS

Peripheral cyanosis causes blue hands and feet, although the mucous membranes of the mouth are pink. Warming the skin on patient's limbs often diminishes peripheral cyanosis because blood flow to the involved area improves, whereas the color of central cyanosis is unchanged or deepens after warming of the skin.

C. PSEUDOCYANOSIS

In patients with pseudocyanosis, the mucous membranes of the mouth are pink, and pressure on the skin fails to blanch the abnormal color.[6]

D. CYANOSIS AND OXIMETRY

Cyanosis affects co-oximetry (i.e., blood gas analysis in the laboratory) differently than it affects pulse oximetry (i.e., equipment used at the bedside; see Chapter 20). Because co-oximetry can distinguish deoxyhemoglobin from other abnormal hemoglobin, it indicates hypoxemia only in patients with central cyanosis (i.e., it samples *arterial* blood and therefore indicates normal oxygen levels in peripheral cyanosis). Pulse oximetry, in contrast, detects the *color* of the pulsatile waveform in the digit. Although it also indicates hypoxemia in patients with central cyanosis, pulse oximetry may falsely indicate arterial hypoxemia in patients with peripheral cyanosis or with abnormal hemoglobin (see Chapter 20). Both co-oximetry and pulse oximetry indicate normal oxygen levels in pseudocyanosis.

IV. CLINICAL SIGNIFICANCE

A. CENTRAL CYANOSIS

Any disorder causing hypoxemia may generate sufficient deoxyhemoglobin in the blood leaving the heart to produce central cyanosis. Typical etiologies are pulmonary edema, pneumonia, and intracardiac right-to-left shunts. The finding of central cyanosis increases greatly the probability of hypoxemia (likelihood ratio [LR] = 7.4; see EBM Box 9.1). Hypoxemia is defined as arterial deoxyhemoglobin level ≥2.38 g/dL, corresponding to SaO_2 ≤80% and pO_2 ≤45 mm Hg in patients with normal amounts of hemoglobin (see Table 9.1). The absence of central cyanosis greatly decreases the likelihood of such severe hypoxemia (LR = 0.2; see EBM Box 9.1).

In patients with chronic liver disease, the finding of cyanosis increases the probability of hepatopulmonary syndrome (LR = 3.6; see Chapter 8).

B. PERIPHERAL CYANOSIS

In clinical practice, common causes of peripheral cyanosis are low cardiac output, arterial disease or obstruction (e.g., Raynaud disease), and venous disease.

C. PSEUDOCYANOSIS

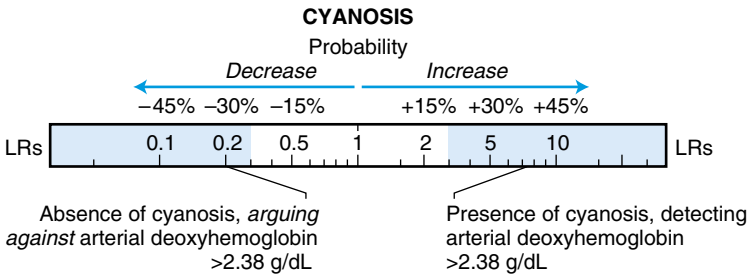
Pseudocyanosis may occur after exposure to metals (*argyria* from topical silver compounds; *chrysiasis* of gold therapy) or drugs (amiodarone, minocycline, chloroquine, or phenothiazines).[10,11]

The references for this chapter can be found on www.expertconsult.com.

EBM BOX 9.1
*Central Cyanosis, Detecting Arterial Deoxyhemoglobin ≥2.38 g/dL**

Finding (Reference)	*Sensitivity (%)*	*Specificity (%)*	Likelihood Ratio† if Finding Is	
			Present	*Absent*
Central cyanosis[2,4]	79-95	72-95	7.4	0.2

*Corresponding to O_2 saturation of 80% and pO_2 of 45 mm Hg if hemoglobin concentration is 12 g/dL (see Table 9.1).
†Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
Click here to access calculator



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